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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,243	11/17/2006	Koji Odan	YAMAPI012US	4126
43/076 7590 03/26/2010 MARK D. SARALINO (GENERAL) RENNER, OTTO, BOISSELLE & SKLAR, LLP 1621 EUCLID AVENUE, NINETEENTH FLOOR CLEVELAND, OH 44115-2191				
EXAMINER HANLEY, SUSAN MARIE				
ART UNIT		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/596,243

Applicant(s)

ODAN ET AL.

Examiner

SUSAN HANLEY

Art Unit

1651

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 6-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 6-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)
- _____ Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
- _____ Paper No(s)/Mail Date _____
- 5) ☐ Notice of Inventor's Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1 and 6-11 remain under examination.

Withdrawal of Rejections

Applicant's arguments, filed 1/7/2010, have been fully considered and they are non-persuasive. The following rejections are reiterated. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 6 and 9-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Fuji et al. (WO 02/097107; cited in the IDS filed 6/6/06) in view Suzuki et al (1983; cited in the IDS filed 12/2/08), Kim et al. (2002) and Nilsson (US 6,077,695) for the reasons given in the last Office action and those stated herein.

Applicant argues that one skilled in the art could not predict the direction of a combination of enzymatic reactions such as that of cellobiose phosphorylase and alpha-glucan phosphorylase wherein there is a simultaneous reaction with a shared substrate and product or have expected the effects of improved yield of alpha-glucan as compared to the reaction when glucose is not removed.

Applicant asserts that the examiner has failed to explain why it would have been expected that in a combined reaction system that the yield of the reaction would be improved when the byproduct is eliminated.

Applicant asserts that Kim teaches that D-glucose competed with G-1-P for the binding site of the synthetic reaction and that one skilled in the art would expect that the reduction of D-glucose would promote the reaction to proceed in the direction of cellobiose synthesis. Applicant argues that the portion of Kim under the heading of "Reaction Mechanism of CBP" does not clearly indicate which reaction of the two catalyzed by CBP is inhibited. Applicant asserts that on page 200 on line 14 of the right column that it was observed that D-glucose was the strongest inhibitor referring to the synthetic reaction. Applicant further argues that Kim reports that there is a decrease in initial velocity on the reverse reaction with an increase of the concentration of D-glucose. Applicant concludes from Kim that one skilled in the art would expect that if the glucose concentration of the reaction is decreased that the reverse reaction (the synthetic reaction) would proceed and the synthesis of amylose yield would decrease. Applicant asserts that Kim does not describe or suggest that the removal of glucose would increase the yield of amylose.

Applicant argues that Nilsson describes transglycosylation using a glucosyl enzyme which is a different reaction and enzyme as compared with the present invention.

Applicant points to the instant specification to show that it was demonstrated that in the production of sucrose from cellobiose, the removal of glucose from the reaction system did not improve the yield of sucrose significantly. Applicant concludes that the combined teachings fail to address the problem to be solved, the claimed mechanism to arrive at the solution and the effect contained therein.

Applicant's arguments have been considered but they are not persuasive.

Responding to Applicant's argument that one could not predict the direction of a combination of enzymatic reactions such as the combination of cellobiose phosphorylase and alpha-glucan phosphorylase, the ordinary artisan knew from Fuji and Suzaki that CBP produces glucose and G-1-P and that sucrose phosphorylase (SP) uses the product of the reaction of CBP, G-1-P to produce chain extended amylose. Thus, the ordinary artisan would have known that putting the two enzymes together in one pot with cellobiose and a source of phosphate would produce chain extended amylose since the product of the CBP reaction is the substrate for the SP reaction.

Responding to Applicant's argument that one of skill in the art would not have expected the effects of improved yield of alpha-glucan as compared to the reaction when glucose is not removed or that Nilsson is not relevant to the rejection, Kim demonstrated that the activity of CBP is inhibited by glucose. Hence, the ordinary artisan would have realized that removal of the interfering product would increase the yield of amylose. Nilsson teaches that if high concentrations of cellobiose are used in the transglycosylation process, considerable amounts of glucose as a byproduct of the

reaction will be formed. The formed glucose will compete with the acceptor and water for the glucosyl-enzyme intermediate, thus inhibiting the synthesis of the desired product. The addition of isomerase or an oxidase can be used to remove the inhibitory glucose during the reaction to improve product yield (col. 7, lines 54-68). Thus, Nilsson teaches an enzyme system having a similar problem (glucose byproduct inhibits the desired reaction) and a solution to that problem (removal of the by-product).

Responding to Applicant's arguments regarding Kim, under the heading of "Reaction Mechanism of CBP", Kim is discussing the conversion of cellobiose to glucose and G-1-P because he refers to the double reciprocal plots of the initial velocities of the substrates (cellobiose and P_i) wherein the crossing of the lines indicates that the reaction is sequential bi bi. That is, P_i first binds to the enzyme followed by cellobiose and glucose and then G-1-P are released (Scheme 1). Kim then reports that "the inhibition patterns of the products, G-1-P and glucose, against the substrate D-cellobiose and P_i , are shown in Fig 3. G-1-P acted as a competitive inhibitor against P_i (Fig. 3B), whereas others (Fig. 3 A, C and D) showed mixed type inhibition patterns". "Increasing concentration of glucose clearly inhibits the velocity of the forward (breakdown) reaction (Fig. 3C).

Regarding Kim's disclosure about the synthetic reaction, reaction conditions are set up specifically to study the reverse (synthetic) reaction. Glucose is an inhibitor along with G-1-P in the back reaction and glucose is also a substrate for the reverse reaction (p. 201, left col.). Substrate inhibition is a well known phenomenon and it occurs at higher concentration of substrate (Fig. 6). Thus, it is not contradictory that glucose

inhibits the reverse reaction at high substrate concentrations when the reaction is being studied in that direction. What the ordinary artisan would have realized is that under conditions in the forward reaction, glucose clearly inhibits the break down of cellobiose. Thus, it is an inhibitor of the forward reaction and there is a clear advantage to keeping the reaction going in the forward direction if the product, glucose, can be removed to prevent it from accumulating to inhibitory levels.

Responding to Applicant's argument that the synthesis of sucrose from cellobiose did not display inhibition from glucose, that is a different reaction system compared to what is being claimed. The ordinary artisan would have known from Kim that the build up of glucose from the breakdown of cellobiose results in inhibition of CBP. Hence, there is a clear advantage to removing the glucose by-product in order to keep the reaction going in that direction.

Responding to Applicant's conclusion, the ordinary artisan would have realized the problem at hand (that glucose build up inhibits the breakdown of cellobiose by CBP) and that removal of glucose prevents this inhibition. Nilsson discloses a reaction system having a similar problem (glucose byproduct inhibits the desired reaction) and a solution (removal of glucose by converting it into a non-competing product).

Claims 1 and 6-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Fuji et al. (WO 02/097107; cited in the IDS filed 6/6/06) in view of Suzaki et al. (1983; cited in the IDS filed 12/2/08), Kim et al. (2002), Wada et al. (JP 2003093090;

machine translation) and Taguchi et al. (1994, abstract only) for the reasons given in the previous Office reaction and those discussed herein.

Applicant argues that the examiner has failed to consider whether by combining references the skilled artisan would have expected a solution where the reactions occur simultaneously to attain the claimed effects. Applicant asserts that the examiner has not explained why it would have been expected in a complicated reaction system that combined two phosphorylated, that the reaction yield would be improved even with the by-product is eliminated. Applicant asserts that the improvement seen by Wada is only 2% compared to that which is disclosed. Applicant asserts that the result of the present invention is unexpectedly significant. Applicant points out that different enzymatic reactions and enzyme are used.

Applicant argues that 1,5-anhydroglucitol is oxidized by using glucose-2-oxidase to generate hydrogen peroxide. If the blood contains glucose, the glucose is also oxidized to hydrogen peroxide by glucose-2-oxidase. Applicant asserts that in Taguchi, the blood glucose does not interfere with the enzymatic reaction but interferes with the measurement of the byproduct of hydrogen peroxide. Applicant concludes that the combined teaching fails to address the problem to be solved, the claimed mechanism to arrive at the solution and the effect contained therein.

Applicant's argument has been considered but it is non-persuasive.

Responding to Applicant's assertion that the examiner has failed to consider whether by combining references the skilled artisan would have expected a solution

where the reactions occur simultaneously to attain the claimed effects, Wada shows that glucose can be removed while other enzymatic reactions are occurring.

Responding to Applicant's argument regarding the complex nature of the system and that the skilled artisan would not have expected an improvement even when glucose is eliminated from the system, the ordinary artisan knew from Fuji and Suzaki that CBP produces glucose and G-1-P and that sucrose phosphorylase (SP) uses the product of the reaction of CBP, G-1-P to produce chain extended amylose. Thus, the ordinary artisan would have known that putting the two enzymes together in one pot with cellobiose and a source of phosphate would produce chain extended amylose since the product of the CBP reaction is the substrata for the SP reaction. From Kim, the ordinary artisan would have known that CBP is inhibited by glucose and from Wada that is desirable to remove glucose when it is a byproduct in the enzymatic conversion of sucrose to inulin because it will increase the yield of the desired product.

Regarding Applicant's argument regarding the improvement in yield experienced by Wada and the alleged unexpected results, as Applicant points out, the Wada system is a different set of enzymatic reactions compared to that which is claimed. Hence, the increase in yield is dependent upon the particular set of enzymes used. However, the ordinary artisan would reasonably have expected an increased yield in coupled CBP/SP system as claimed since the by-product, glucose, is being removed so it can no longer inhibit the CBP forward reaction.

Regarding Applicant's argument regarding Taguchi, the generation of hydrogen peroxide by glucose does interfere with the measurement of 1,5-anhydroglucitol. That is

why Taguchi first removes glucose from the blood sample by adding glucose oxidase, mutarotase and catalase. Glucose is converted into glucono-gamma-lactone and the catalase removes the peroxide by-product of the glucose oxidase reaction. (Hence, this is another example of removing an interfering by product by converting the interfering by-product to another non-interfering entity). The enzymes are removed by contact with a gel and the lactone is converted to gluconic acid in the supernatant. After this procedure, the 1,5-anhydroglucitol is then measured by oxidation with glucose-2-oxidase and the hydrogen peroxide generated from this reaction is then measured. Thus, the initial addition of glucose-1-oxidase, mutarotase and catalase rids the sample of glucose so that the assay of 1,5-anhydroglucitol can proceed.

Responding to Applicant's conclusion, the ordinary artisan would have realized the problem at hand (that glucose build up inhibits the breakdown of cellobiose by CBP) and that removal of glucose prevents this inhibition. Wada discloses a reaction system having a similar problem (glucose byproduct inhibits the desired reaction) and a solution (removal of glucose by converting it into a non-competing product). Taguchi provides another enzyme system that can convert glucose into a non-interfering product.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/
Primary Examiner, Art Unit 1651

/Susan Hanley/
Examiner, Art Unit 1651